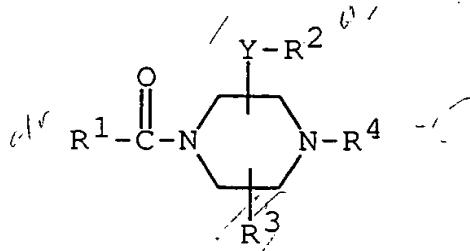


C L A I M S

1. A compound of the formula :

5



10

wherein

Y is bond or lower alkylene,

R¹ is aryl which may have substituent(s),R² is aryl or indolyl, each of which may have substituent(s),R³ is hydrogen or lower alkyl,R⁴ is pyridyl(lower)alkylamino(lower)alkynyl;

N-(lower alkyl)-N-[pyridyl(lower)alkyl]amino-(lower)alkyl;

hydroxy(lower)alkoxy(lower)alkyl;

lower alkanoyl(lower)alkoxy(lower)alkyl;

phenyl(lower)alkyl which has hydroxy(lower)alkyl or morpholinyl(lower)alkyl;

ar(lower)alkoxycarbonyl;

(2-pyridyl)(lower)alkyl which may have 1 to 3

substituent(s) selected from the group consisting

of lower alkyl, lower alkoxy, lower aloxycarbonyl, mono(or di or tri)halo(lower)alkyl and halogen;

(3-pyridyl)propyl which may have lower alkoxy or amino;

(3-pyridyl)butyl which may have lower alkoxy or amino;

pyridyl(lower)alkenyl which may have (lower alkoxy or amino)

(2-pyridyl)(lower)alkynyl which (may have 1 to 3

25

30

35

substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkoxycarbonyl, mono(or di or tri)halo(lower)alkyl and halogen; (3-pyridyl)-(lower)alkynyl which may have lower

✓ alkoxy or amino;

pyridyl, thiazolyl, imidazolyl or pyrazolyl, each of which may have substituent(s);

imidazolyl(lower)alkyl which may have 1 or 2

substituent(s) selected from the group consisting of lower alkyl, lower alkynyl, ar(lower)alkyl, pyridyl(lower)alkyl, mono(or di or tri)halo(lower)alkyl and halogen;

pyrazolyl(lower)alkyl which may have

hydroxy(lower)alkyl, carboxy(lower)alkyl, lower

alkoxycarbonyl(lower)alkyl, morpholinyl(lower)alkyl
or morpholinylcarbonyl(lower)alkyl;

thiazolyl(lower)alkyl which may have lower alkyl;

piperidyl(lower)alkyl which may have

hydroxy(lower)alkyl or lower alkoxy;

morpholinyl(lower)alkyl which has 1 or 2

substituent(s) selected from the group consisting of ethyl, hydroxy(lower)alkyl, halo(lower)alkyl and lower alkoxy(lower)alkyl;

morpholinyl(lower)alkyl which has lower alkyl and lower alkoxy(lower)alkyl;

(3,5-dimethylmorpholino) (lower) alkyl;

morpholino(lower)alkenyl which may have lower alkyl or lower alkoxy(lower)alkyl;

(2- or 3-morpholinyl)(lower)alkenyl which may have lower alkoxy carbonyl;

pyrrolidinyl(lower)alkynyl which may have lower alkoxy(lower)alkyl;

morpholinyl(lower)alkynyl which may have 1 or 2 substituent(s) selected from the group consisting of

of ethyl, propyl, isopropyl, isobutyl,

spirocyclo(lower)alkyl, lower alkoxy(lower)alkyl,
hydroxy(lower)alkyl, carboxy(lower)alkyl,
di(lower alkyl)carbamoyl, lower alkoxycarbonyl and
halo(lower)alkyl;

5 morpholinyl(lower)alkynyl which has methyl and
lower alkoxy;

(dimethylmorpholino)(lower)alkynyl;

homomorpholinyl(lower)alkynyl which have halogen;

10 (morpholinylamino)propyl which may have lower
alkanoyl;

thiomorpholinyl(lower)alkynyl which may have
substituent(s);

homomorpholinylamino(lower)alkyl;

thiomorpholinylamino(lower)alkyl; or

saturated heterocyclicimino(lower)alkyl,

15 \hookrightarrow saturated heterocyclicaminocarbonyl(lower)alkyl or
saturated heterocyclic(lower)alkoxy(lower)alkyl,
each of which may have substituent(s),

20 \rightarrow provided that when

R^4 is 2-[N-methyl-N-(3-pyridylmethyl)amino]ethyl,

3-(3-pyridyl)propyl,

3-(3-pyridyl)-2-propynyl,

4-[(2-methoxymethyl)pyrrolidino]-2-butynyl,

4-thiomorpholino-2-butynyl,

25 3-(morpholinoamino)propyl,

4-morpholino-2-butenyl,

4-morpholino-2-butynyl, or

4-(3,3-dimethylmorpholino)-2-butynyl, then

20 R^1 is not 3,5-bis(trifluoromethyl)phenyl,

30 and a salt thereof.

2. The compound of claim 1, in which

Y is lower alkylene,

35 R^1 is C_6-C_{10} aryl which may have 1 or 2 substituent(s)
selected from the group consisting of mono(or di

))

N / or tri)halo(lower)alkyl, halogen, lower alkylamino, di(lower)alkylamino and nitro,

5 R² is C₆-C₁₀ aryl or indolyl, each of which may have 1 to 3 substituent(s) selected from the group consisting of lower alkyl, mono(or di or tri)halo(lower)alkyl, lower alkylenedioxy, hydroxy, hydroxy(lower)alkyl, lower alkoxy, lower alkylamino and di(lower)alkylamino,

10 R³ is hydrogen, and

15 R⁴ is pyridyl(lower)alkylamino(lower)alkynyl; (2-pyridyl)propyl which may have 1 to 3 substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, [lower alkoxycarbonyl], mono(or di or tri)halo(lower)alkyl and halogen; pyridyl, thiazolyl, imidazolyl or pyrazolyl, each of which may have 1 or 2 substituent(s) selected from the group consisting of lower alkyl, ar(lower)alkyl and pyridyl(lower)alkyl; imidazolyl(lower)alkyl which has 1 or 2

20 substituent(s) selected from the group consisting (of lower alkyl) lower alkynyl, ar(lower)alkyl, pyridyl(lower)alkyl, mono(or di or tri)halo(lower)alkyl and halogen;

25 (2-methyl-1H-imidazol-4-yl)(lower)alkyl which has 1 or 2 substituent(s) selected from the group consisting of isopropyl, lower alkynyl, ar(lower)alkyl, pyridyl(lower)alkyl, mono(or di or tri)halo(lower)alkyl and halogen;

30 (5-methyl-1H-imidazol-4-yl)(lower)alkyl which has 1 or 2 substituent(s) selected from the group consisting of isopropyl, lower alkynyl, ar(lower)alkyl, pyridyl(lower)alkyl, mono(or di or tri)halo(lower)alkyl and halogen;

35 N [piperidyl(lower)alkyl which may have hydroxy(lower)alkyl or lower alkoxy;

✓ morpholinyl(lower)alkyl which has 1 or 2
5 substituent(s) selected from the group consisting
of ethyl, hydroxy(lower)alkyl, halo(lower)alkyl and
lower alkoxy(lower)alkyl;
morpholinyl(lower)alkyl which has lower alkyl and
lower alkoxy(lower)alkyl;
✓ (3,5-dimethylmorpholino)(lower)alkyl;
morpholino(lower)alkenyl which may have lower alkyl
10 or lower alkoxy(lower)alkyl;
✓ (2- or 3-morpholinyl)(lower)alkenyl which may have
lower alkoxycarbonyl;
pyrrolidinyl(lower)alkynyl which may have lower
15 alkoxy(lower)alkyl;
morpholinyl(lower)alkynyl which may have 1 or 2
✓ substituent(s) selected from the group consisting
of ethyl, propyl, isopropyl, isobutyl,
spirocyclo(lower)alkyl, lower alkoxy(lower)alkyl,
20 hydroxy(lower)alkyl, carboxy(lower)alkyl, di(lower
alkyl)carbamoyl, lower alkoxycarbonyl and
halo(lower)alkyl;
morpholinyl(lower)alkynyl which has methyl and
lower alkoxy(lower)alkyl;
(dimethylmorpholino)(lower)alkynyl; or
25 homomorpholinyl(lower)alkynyl which may have
halogen.

3. The compound of claim 2, in which
Y is lower alkylene,
R¹ is phenyl which has 1 or 2 substituent(s) selected
30 from the group consisting of trihalo(lower)alkyl,
halogen, lower alkylamino, di(lower)alkylamino and
nitro,
R² is phenyl or indolyl, each of which have 1 or 2
35 substituent(s) selected from the group consisting
of lower alkyl, trihalo(lower)alkyl, lower

alkylenedioxy, hydroxy, hydroxy(lower)alkyl, lower alkoxy, lower alkylamino and di(lower)alkylamino,

5 R³ is hydrogen, and

R⁴ is (2-pyridyl)propyl which may have 1 to 3

10 substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, mono(or di or tri)halo(lower)alkyl and halogen;

15 ✓ morpholinyl(lower)alkyl which has 1 or 2 substituent(s) selected from the group consisting

20 of ethyl, hydroxy(lower)alkyl, halo(lower)alkyl and lower alkoxy(lower)alkyl;

25 ✓ morpholinyl(lower)alkynyl which may have 1 or 2 substituent(s) selected from the group consisting

30 of ethyl, propyl, isopropyl, isobutyl,

35 ✓ spirocyclo(lower)alkyl, lower alkoxy(lower)alkyl, hydroxy(lower)alkyl, carboxy(lower)alkyl, di(lower alkyl)carbamoyl, lower alkoxycarbonyl and halo(lower)alkyl.

Compound

20 4. A compound of claim 3, which is selected from the group consisting of

25 (1) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[4-((3S)-3-ethylmorpholino)-2-butynyl]-2-[(1H-indol-3-yl)methyl]piperazine,

30 (2) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3,4-dimethylbenzyl)-4-[2-((2S)-2-methoxymethylmorpholino)ethyl]piperazine,

(3) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3,4-dimethylbenzyl)-4-[2-((3R)-3-methoxymethylmorpholino)ethyl]piperazine,

(4) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3,4-dimethylbenzyl)-4-[2-((2R)-2-methoxymethylmorpholino)ethyl]piperazine,

(5) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-[(1H-indol-3-yl)methyl]-4-[2-((2S)-2-methoxymethyl-

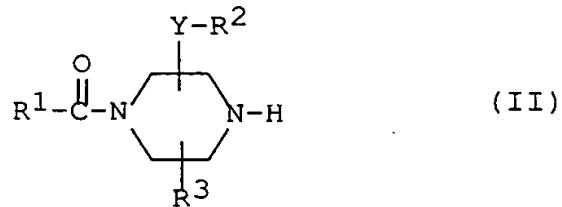
morpholino)ethyl]piperazine, and

(6) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-((3R)-3-ethylmorpholino)ethyl]-2-[(1H-indol-3-yl)-methyl]piperazine

5 or a pharmaceutically acceptable salt thereof.

5. A process for the preparation of the compound of claim 1 or a salt thereof, which comprises,

10 (1) reacting a compound of the formula (II) :



wherein R¹, R², R³ and Y are each as defined in claim 1, or a salt thereof, with a compound of the formula (III) :

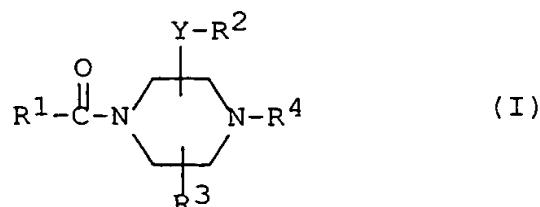


wherein R⁴ is as defined in claim 1 and

25 W₁ is a leaving group,

or a salt thereof to give a compound of the formula

(I) :

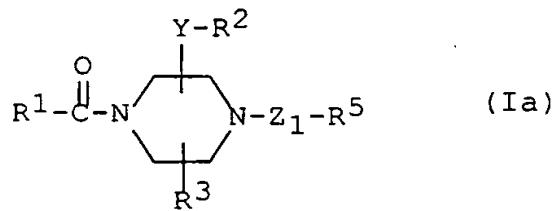


35 wherein R¹, R², R³, R⁴ and Y are each as defined in

claim 1, or a salt thereof,

(2) subjecting a compound of the formula (Ia) :

5



10

wherein R¹, R², R³ and Y are each as defined above,
 R⁵ is 2-pyridyl which may have 1 to 3
 substituent(s) selected from the group
 consisting of lower alkyl, lower alkoxy,
 lower alkoxy carbonyl, mono(or di or
 tri)halo(lower)alkyl and halogen; or
 3-pyridyl which may have lower alkoxy or
 amino, and

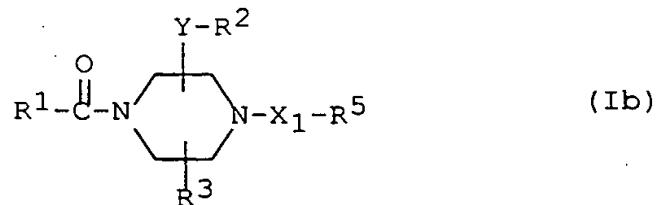
15

Z₁ is lower alkynylene,

20

or a salt thereof to a reduction reaction to give a
 compound of the formula (Ib) :

25



30

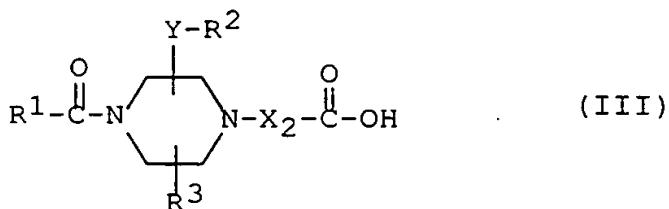
wherein R¹, R², R³, Y and R⁵ are each as defined above,
 and

X₁ is lower alkylene,

or a salt thereof,

35

(3) reacting a compound of the formula (III) :

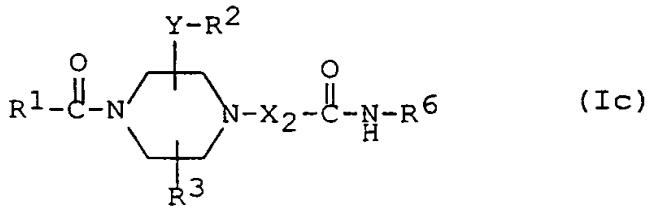


wherein R^1 , R^2 , R^3 and Y are each as defined above,
and

10 X_2 is lower alkylene,
or its reactive derivative at the carboxy group or a
salt thereof with a compound of the formula (V) :

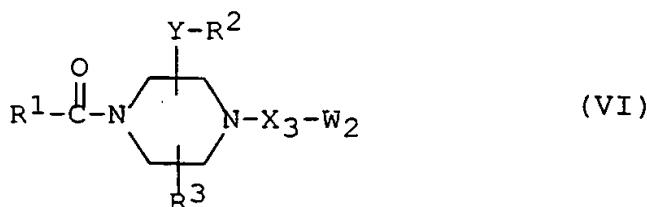


wherein R^6 is saturated heterocyclic which may have
substituent(s),
or a salt thereof to give a compound (Ic) :



25 wherein R^1 , R^2 , R^3 , R^6 , X_2 and Y are each as defined
above,

30 (4) reacting a compound of the formula (VI) :



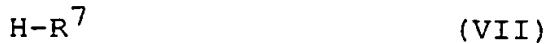
wherein R^1 , R^2 , R^3 and Y are each as defined above,

X_3 is lower alkylene and

W_2 is a leaving group,

or a salt thereof with a compound of the formula

5 (VII) :



wherein R^7 is pyridyl(lower)alkylamino;

N-(lower alkyl)-N-[pyridyl(lower)alkyl]-
amino;

10 1-imidazolyl which may have 1 or 2
substituent(s) selected from the group
consisting of lower alkyl, lower alkynyl,
ar(lower)alkyl, pyridyl(lower)alkyl,
mono(or di or tri)halo(lower)alkyl and
halogen;

15 1-pyrazolyl which may have
hydroxy(lower)alkyl, carboxy(lower)alkyl,
lower alkoxy carbonyl(lower)alkyl,
morpholinyl(lower)alkyl or
morpholinyl carbonyl(lower)alkyl;
piperidino which may have
hydroxy(lower)alkyl or lower alkoxy;

20 morpholino which has 1 or 2
substituent(s) selected from the group
consisting of ethyl, hydroxy(lower)alkyl,
halo(lower)alkyl and lower alkoxy-
(lower)alkyl;

25 morpholino which has lower alkyl and
lower alkoxy(lower)alkyl;

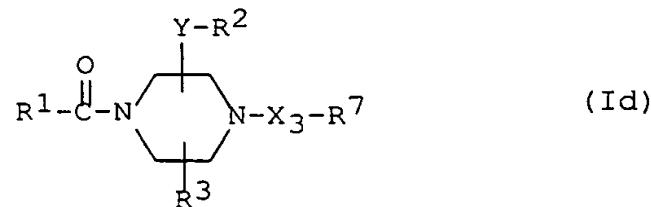
30 3,5-dimethylmorpholino;

morpholinylamino which may have lower
alkanoyl;

homomorpholinylamino; or
thiomorpholinylamino,

35 or a salt thereof to give a compound of the formula

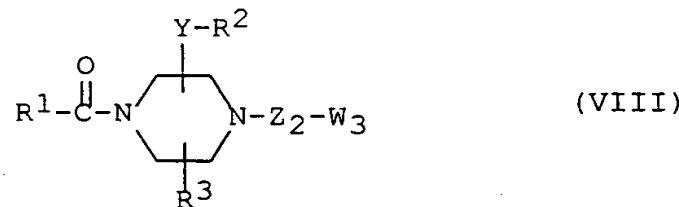
(Id) :



wherein R^1 , R^2 , R^3 , R^7 , X_3 and Y are each as defined above,

10 or a salt thereof,

(5) reacting a compound of the formula (VIII) :



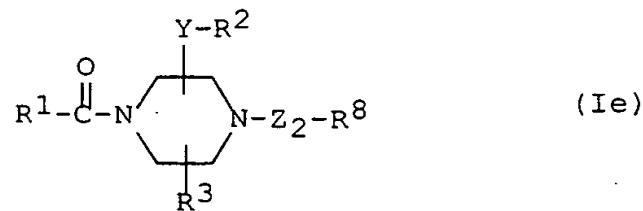
20 wherein R^1 , R^2 , R^3 and Y are each as defined above,
 Z_2 is lower alkenylene, and
 W_3 is a leaving group,

or a salt thereof with a compound of the formula (IX) :



wherein R^8 is morpholino which may have lower alkyl or lower alkoxy(lower)alkyl,

or a salt thereof to give a compound of the formula
30 (Ie) :

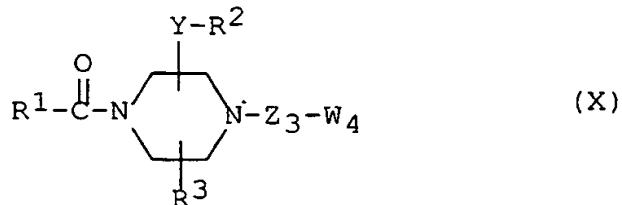


wherein R^1 , R^2 , R^3 , R^8 , Y and Z_2 are as defined as above,

or a salt thereof,

5 (6) reacting compound of the formula (X) :

10



15

wherein R^1 , R^2 , R^3 and Y are each as defined above,

Z_3 is a lower alkynylene and

W_4 is a leaving group,

or a salt thereof with a compound of the formula (XI) :

20



25

wherein R^9 is pyrrolidino which may have lower alkoxy(lower)alkyl; morpholino which may have 1 or 2 substituent(s) selected from the group consisting of ethyl, propyl, isopropyl, isobutyl, spirocyclo(lower)alkyl, lower alkoxy(lower)alkyl, hydroxy(lower)alkyl, carboxy(lower)alkyl, di(lower alkyl)carbamoyl, lower alkoxy carbonyl and halo(lower)alkyl;

30

morpholino which has methyl and lower alkoxy;

dimethylmorpholino; or

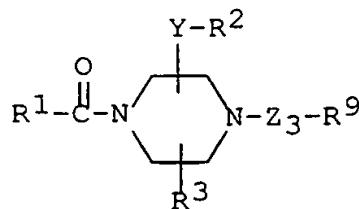
homomorpholino which has halogen,

35

or a salt thereof to give a compound of the formula

(If) :

5



(If)

10

wherein R¹, R², R³, R⁹, Y and Z₃ are each as defined
above,
or a salt thereof.

15

6. A pharmaceutical composition which comprises, as an active ingredient, a compound of claim 1 or a pharmaceutically acceptable salt thereof in admixture with pharmaceutically acceptable carriers.

20

7. A compound of claim 1 for use as a medicament.

25

8. A method for treating or preventing Tachykinin-mediated diseases which comprises administering an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof to human being or animals.

30

9. A compound of claim 1 for use as Tachykinin antagonist.

10. Use of a compound of claim 1 for manufacture of a medicament for treating or preventing Tachykinin-mediated diseases.